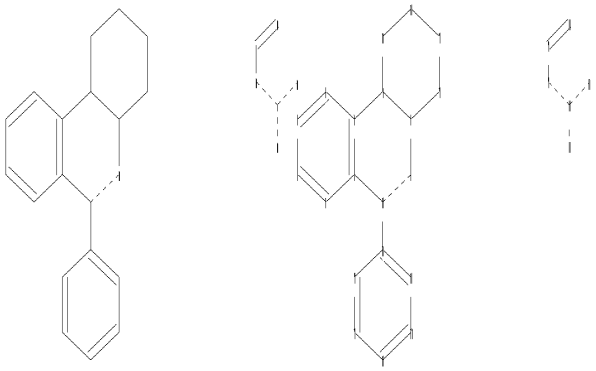
=>
Uploading C:\Program Files\Stnexp\Queries\10589082.str



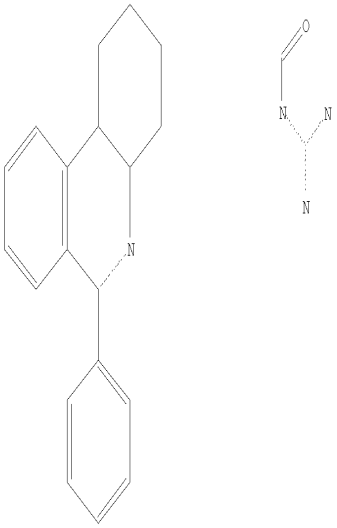
chain nodes :
21 22 24
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
ring/chain nodes :
23 25 26
chain bonds :
10-15 21-22 21-23 22-24 24-25 24-26
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 7-11 8-9 8-14 9-10 11-12 12-13
13-14 15-16 15-20 16-17 17-18 18-19 19-20
exact/norm bonds :
5-7 6-10 7-8 7-11 8-9 8-14 9-10 11-12 12-13 13-14 21-22 21-23 22-24
24-25 24-26
exact bonds :
10-15
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 15-16 15-20 16-17 17-18 18-19 19-20

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:CLASS
22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 18:29:20 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 9 TO ITERATE

100.0% PROCESSED 9 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 9 TO 360
PROJECTED ANSWERS: 2 TO 124

L2 2 SEA SSS SAM L1

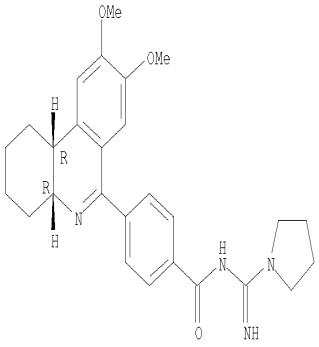
=> dscan
DSCAN IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> d scan

L2 2 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, 4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-

phenanthridinyl]-N-(imino-1-pyrrolidinylmethyl)-
MF C27 H32 N4 O3

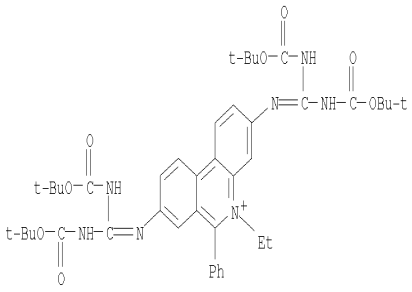
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L2 2 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Phenanthridinium, 3,8-bis[[bis[[(1,1-dimethylethoxy)carbonyl]amino]methylene]amino]-5-ethyl-6-phenyl-
MF C43 H56 N7 O8
CI COM



ALL ANSWERS HAVE BEEN SCANNED

=> d his

(FILE 'HOME' ENTERED AT 18:28:42 ON 03 MAR 2008)

FILE 'REGISTRY' ENTERED AT 18:29:00 ON 03 MAR 2008
L1 STRUCTURE UPLOADED
L2 2 S L1

=> s l1 full
FULL SEARCH INITIATED 18:29:51 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 167 TO ITERATE

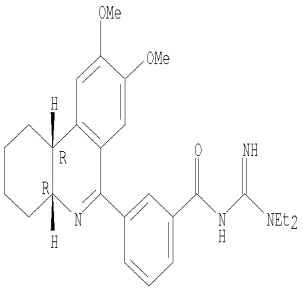
100.0% PROCESSED 167 ITERATIONS 25 ANSWERS
SEARCH TIME: 00.00.01

L3 25 SEA SSS FUL L1

=> d scan

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, N-[(diethylamino)iminomethyl]-3-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-
MF C27 H34 N4 O3

Absolute stereochemistry.

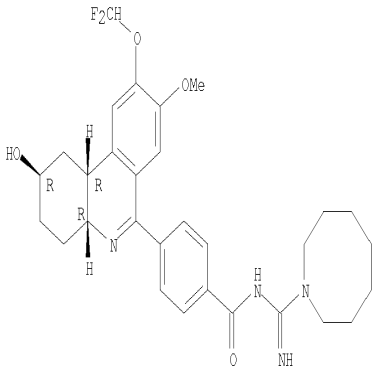


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2000

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, 4-[(2R,4aR,10bR)-9-(difluoromethoxy)-1,2,3,4,4a,10b-hexahydro-2-hydroxy-8-methoxy-6-phenanthridinyl]-N-[(hexahydro-1(2H)-azocinyl)iminomethyl]-, rel-
MF C30 H36 F2 N4 O4

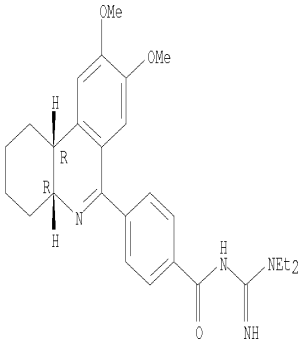
Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, N-[(diethylamino)iminomethyl]-4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-
MF C27 H34 N4 O3

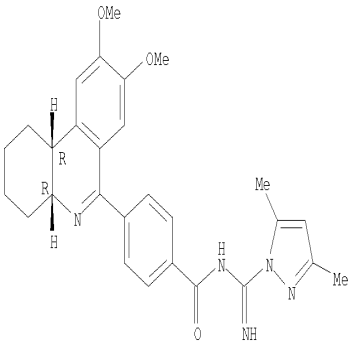
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, N-[(3,5-dimethyl-1H-pyrazol-1-yl)iminomethyl]-4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-
MF C28 H31 N5 O3

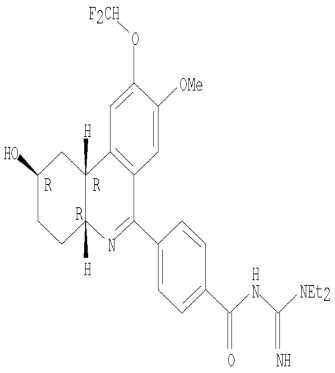
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

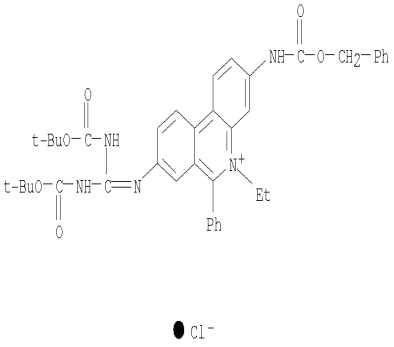
L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, N-[(diethylamino)iminomethyl]-4-[(2R,4aR,10bR)-9-(difluoromethoxy)-1,2,3,4,4a,10b-hexahydro-2-hydroxy-8-methoxy-6-phenanthridinyl]-, rel-
MF C27 H32 F2 N4 O4

Relative stereochemistry.



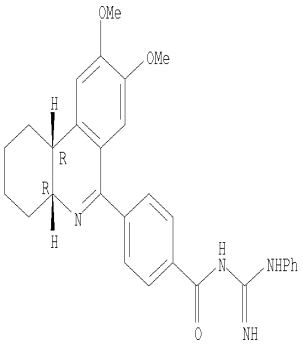
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Phenanthridinium, 8-[[bis[[(1,1-dimethylethoxy)carbonyl]amino]methylene]amino]-5-ethyl-6-phenyl-3-[[(phenylmethoxy)carbonyl]amino]-, chloride (9CI)
MF C40 H44 N5 O6 . Cl



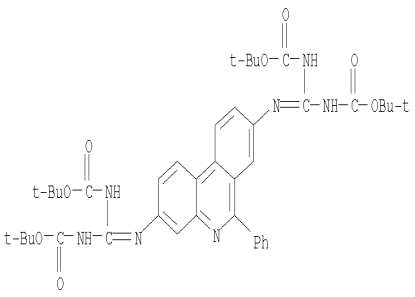
L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, 4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-[imino(phenylamino)methyl]-
MF C29 H30 N4 O3

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

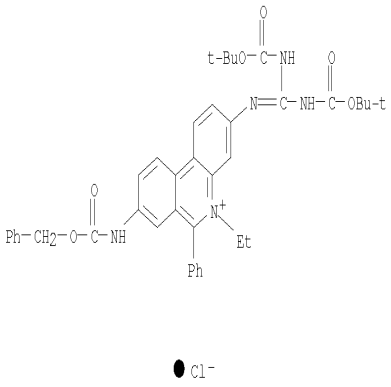
L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Carbamic acid, [(6-phenyl-3,8-phenanthridinediyl)bis(nitrilomethanetetrayl)]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI)
MF C41 H51 N7 O8



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

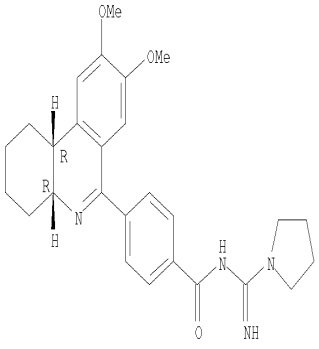
L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Phenanthridinium, 3-[[bis[[(1,1-dimethylethoxy)carbonyl]amino]methylene]amino]-5-ethyl-6-phenyl-8-[[(phenylmethoxy)carbonyl]amino]-, chloride (9CI)

MF C40 H44 N5 O6 . Cl



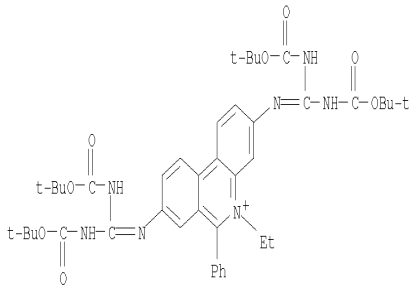
L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, 4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-(imino-1-pyrrolidinylmethyl)-
MF C27 H32 N4 O3

Absolute stereochemistry.



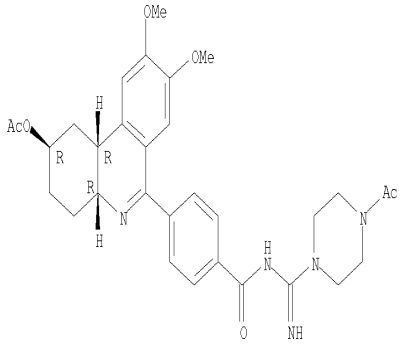
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Phenanthridinium, 3,8-bis[[bis[[(1,1-dimethylethoxy)carbonyl]amino]methylene]amino]-5-ethyl-6-phenyl-
MF C43 H56 N7 O8
CI COM



L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, 4-[(2R,4aR,10bR)-2-(acetyloxy)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-[(4-acetyl-1-piperazinyl)iminomethyl]-, rel-
MF C31 H37 N5 O6

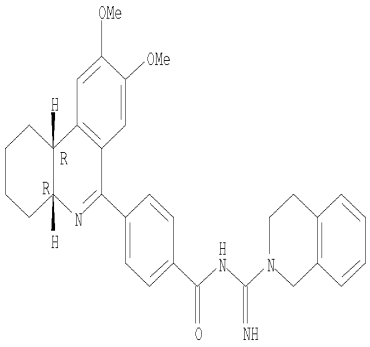
Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

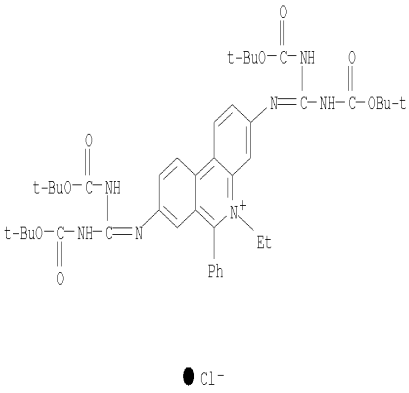
L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, N-[(3,4-dihydro-2(1H)-isoquinolinyl)iminomethyl]-4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-
MF C32 H34 N4 O3

Absolute stereochemistry.



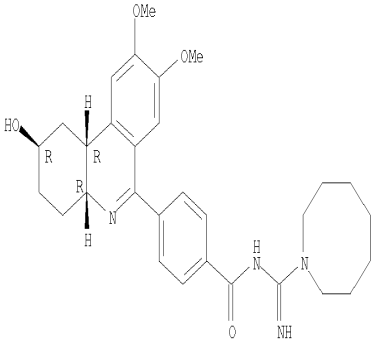
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Phenanthridinium, 3,8-bis[[bis[[(1,1-dimethylethoxy)carbonyl]amino]methylene]amino]-5-ethyl-6-phenyl-, chloride (9CI)
MF C43 H56 N7 O8 . Cl



L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, N-[(hexahydro-1(2H)-azocinyl)iminomethyl]-4-[(2R,4aR,10bR)-1,2,3,4,4a,10b-hexahydro-2-hydroxy-8,9-dimethoxy-6-phenanthridinyl]-, rel-
MF C30 H38 N4 O4

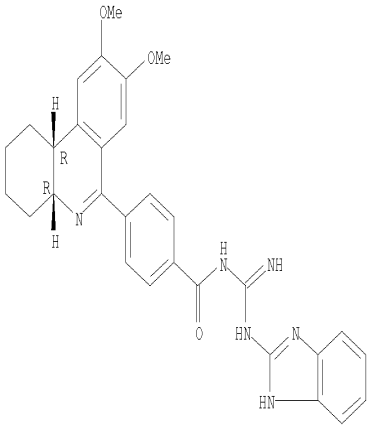
Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

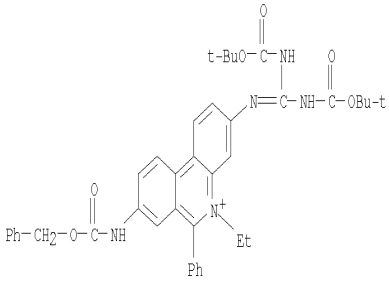
L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, N-[amino(1H-benzimidazol-2-ylamino)methylene]-4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]- (9CI)
MF C30 H30 N6 O3

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

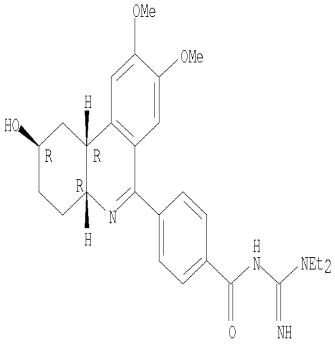
L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Phenanthridinium, 3-[[bis[[(1,1-dimethylethoxy)carbonyl]amino]methylene]amino]-5-ethyl-6-phenyl-8-[[(phenylmethoxy)carbonyl]amino]-
MF C40 H44 N5 O6
CI COM



L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, N-[(diethylamino)iminomethyl]-4-[(2R,4aR,10bR)-1,2,3,4,4a,10b-hexahydro-2-hydroxy-8,9-dimethoxy-6-phenanthridinyl]-, rel-

MF C27 H34 N4 O4

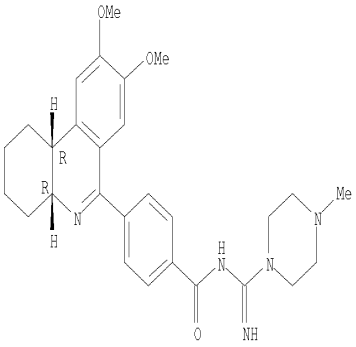
Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

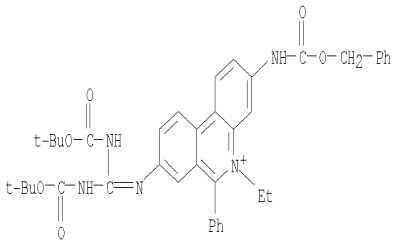
L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, 4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-[imino(4-methyl-1-piperazinyl)methyl]-
MF C28 H35 N5 O3

Absolute stereochemistry.



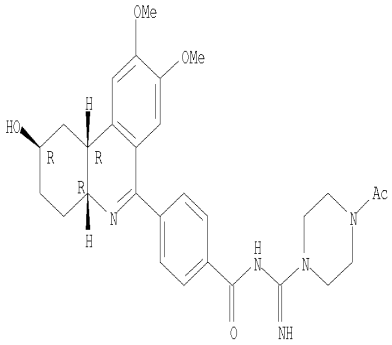
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Phenanthridinium, 8-[[bis[[(1,1-dimethylethoxy)carbonyl]amino]methylene]amino]-5-ethyl-6-phenyl-3-[[(phenylmethoxy)carbonyl]amino]-
MF C40 H44 N5 O6
CI COM



L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, N-[(4-acetyl-1-piperazinyl)iminomethyl]-4-[(2R,4aR,10bR)-1,2,3,4,4a,10b-hexahydro-2-hydroxy-8,9-dimethoxy-6-phenanthridinyl]-, rel-
MF C29 H35 N5 O5

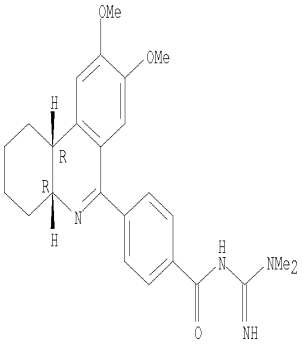
Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, N-[(dimethylamino)iminomethyl]-4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-
MF C25 H30 N4 O3

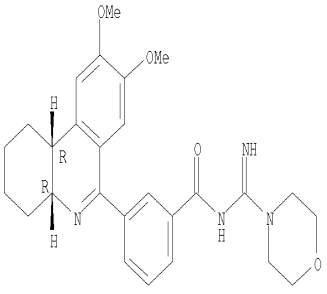
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, 3-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-(imino-4-morpholinylmethyl)-
MF C27 H32 N4 O4

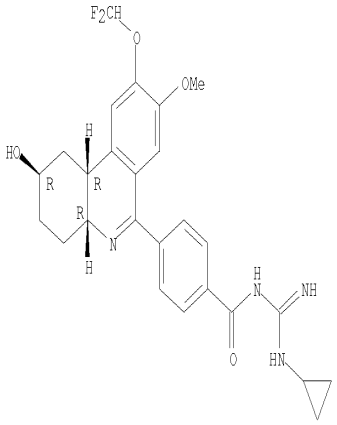
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, N-[(cyclopropylamino)iminomethyl]-4-[(2R,4aR,10bR)-9-(difluoromethoxy)-1,2,3,4,4a,10b-hexahydro-2-hydroxy-8-methoxy-6-phenanthridinyl]-, rel-
MF C26 H28 F2 N4 O4

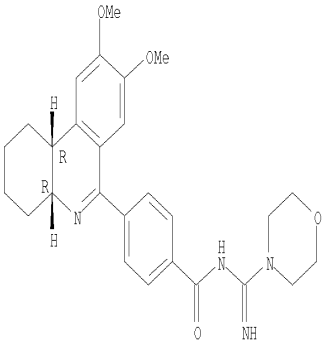
Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, 4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-(imino-4-morpholinylmethyl)-
MF C27 H32 N4 O4

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=> file caplus
FILE 'CAPLUS' ENTERED AT 18:30:14 ON 03 MAR 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 3 Mar 2008 VOL 148 ISS 10
FILE LAST UPDATED: 2 Mar 2008 (20080302/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l3
L4 5 L3

=> d cbib abs hitstr 1-5

L4 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

2005:902858 Document No. 143:248297 Preparation of guanidinyl hydroxyphenylphenanthridines as PDE4 inhibitors. Schmidt, Beate; Flockerzi, Dieter; Hatzelmann, Armin; Zitt, Christof; Barsig, Johannes; Marx, Degenhard; Kley, Hans-Peter; Kautz, Ulrich (Altana Pharma A.-G., Germany). PCT Int. Appl. WO 2005077906 A1 20050825, 72 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2005-EP50708 20050217. PRIORITY: EP 2004-3592 20040218.

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

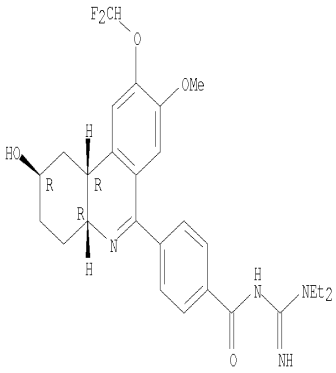
AB Title compds. I [R1 = OH, alkoxy, cycloalkoxy, etc.; R2 = OH, cycloalkylmethoxy, cycloalkoxy, etc. or R1 and R2 together form alkylenedioxy group; R3 = H or alkyl; R4 = OR9 and R5 = H or alkyl or R4 = H or alkyl and R5 = OR9; R6 = H or alkyl; R7 = (un)substituted guanidinyl; R8 = H, halo, nitro, etc.; R9 = H, alkyl, alkoxyalkyl, etc.] and their pharmaceutically acceptable salts, are prepared and disclosed as phosphodiesterase 4 (PDE4) inhibitors. Thus, e.g., II was prepared by coupling of 4-((2RS,4aRS,10bRS)-2-acetoxy-8,9-dimethoxy-1,2,3,4,4a,10b-hexahydro-phenanthridin-6-yl)-benzoic acid with the resp. guanidinyl derivative followed by hydrolysis. The activity of I was evaluated using scintillation proximity assays and it was revealed that selected compds. of the invention displayed -log IC50 values higher than 7.5. I as inhibitor of PDE4 should provide useful in the treatment of respiratory disorders. Pharmaceutical compns. comprising I are disclosed.

IT 862993-72-4P 862993-73-5P 862993-74-6P
862993-75-7P 862993-76-8P 862993-77-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of guanidinyl hydroxyphenylphenanthridines as PDE4 inhibitors)

RN 862993-72-4 CAPLUS

CN Benzamide, N-[(diethylamino)iminomethyl]-4-[(2R,4aR,10bR)-9-(difluoromethoxy)-1,2,3,4,4a,10b-hexahydro-2-hydroxy-8-methoxy-6-phenanthridinyl]-, rel- (CA INDEX NAME)

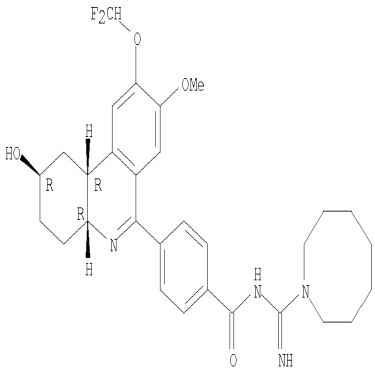
Relative stereochemistry.



RN 862993-73-5 CAPLUS

CN Benzamide, 4-[(2R,4aR,10bR)-9-(difluoromethoxy)-1,2,3,4,4a,10b-hexahydro-2-hydroxy-8-methoxy-6-phenanthridinyl]-N-[(hexahydro-1(2H)-azocinyl)iminomethyl]-, rel- (CA INDEX NAME)

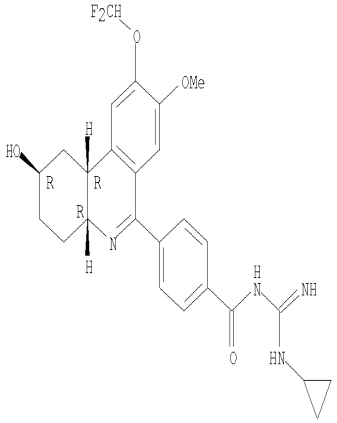
Relative stereochemistry.



RN 862993-74-6 CAPLUS

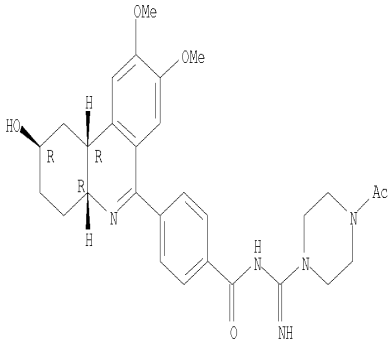
CN Benzamide, N-[(cyclopropylamino)iminomethyl]-4-[(2R,4aR,10bR)-9-(difluoromethoxy)-1,2,3,4,4a,10b-hexahydro-2-hydroxy-8-methoxy-6-phenanthridinyl]-, rel- (CA INDEX NAME)

Relative stereochemistry.



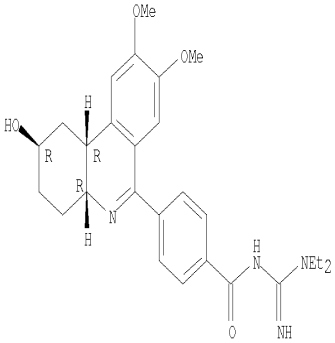
RN 862993-75-7 CAPLUS
CN Benzamide, N-[(4-acetyl-1-piperazinyl)iminomethyl]-4-[(2R,4aR,10bR)-1,2,3,4,4a,10b-hexahydro-2-hydroxy-8,9-dimethoxy-6-phenanthridinyl]-, rel- (CA INDEX NAME)

Relative stereochemistry.



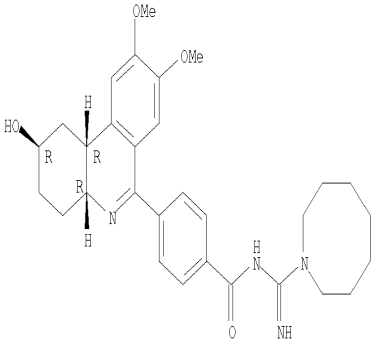
RN 862993-76-8 CAPLUS
CN Benzamide, N-[(diethylamino)iminomethyl]-4-[(2R,4aR,10bR)-1,2,3,4,4a,10b-hexahydro-2-hydroxy-8,9-dimethoxy-6-phenanthridinyl]-, rel- (CA INDEX NAME)

Relative stereochemistry.



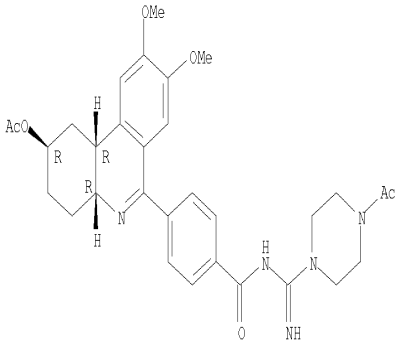
RN 862993-77-9 CAPLUS
CN Benzamide, N-[(hexahydro-1(2H)-azocinyl)iminomethyl]-4-[(2R,4aR,10bR)-1,2,3,4,4a,10b-hexahydro-2-hydroxy-8,9-dimethoxy-6-phenanthridinyl]-, rel- (CA INDEX NAME)

Relative stereochemistry.



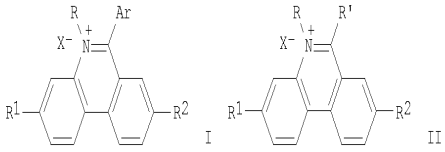
IT 862993-78-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of guanidinyl hydroxyphenylphenanthridines as PDE4 inhibitors)
RN 862993-78-0 CAPLUS
CN Benzamide, 4-[(2R,4aR,10bR)-2-(acetyloxy)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-[(4-acetyl-1-piperazinyl)iminomethyl]-, rel- (CA INDEX NAME)

Relative stereochemistry.



L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
2005:158539 Document No. 142:261402 Preparation of phenanthridine derivatives as anti-viral agents. Tor, Yitzhak; Luedtke, Nathan (The Regents of the University of California, USA). PCT Int. Appl. WO 2005016343 A1 20050224, 58 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US26188 20040811. PRIORITY: US 2003-495445P 20030811.

GI

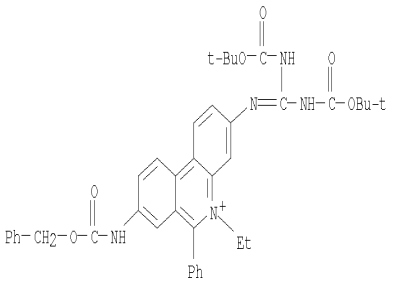


AB A series of substituted phenanthridine derivs. (e.g. ethidium derivs. I and II) (R, R' = each functionalized or unfuctionalized alkyl, alkenyl, alkynyl, aryl, aralkyl, heteroaryl, or alkheteroaryl; wherein alkheteroaryl refers to a straight-chain alkyl, alkenyl or alkynyl group where one of the hydrogen atoms bonded to a terminal carbon atom is replaced with a heteroaryl moiety; Ar = optionally substituted Ph or any aromatic residue; R1, R2 = independently selected from the group consisting of a urea, a substituted urea, a di-Boc-guanidine, conjugated amino acids, carbohydrates, NH2, 1-pyrrolyl, guanidino, and benzyloxycarbonylamino) has been synthesized by converting the amines at the 3- and 8- positions of

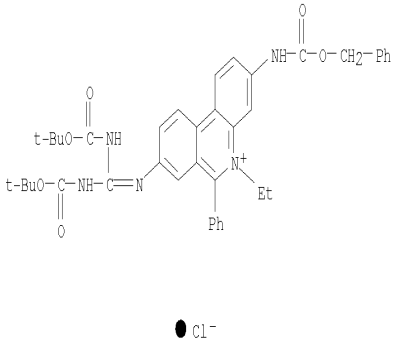
ethidium bromide into guanidine, pyrrole, urea, and various substituted ureas. The resulting derivs. exhibit unique spectral properties that change upon binding nucleic acids. These compds. maximize the binding affinity of phenanthridine to viral RNA and DNA sites, while minimizing the binding to host cell DNA. The antiviral activity of the compds. can thus be maximized, while toxic and/or mutagenic side effects are minimized. The compds. have an enhanced affinity and specificity for HIV-1 rev response element as compared to ethidium bromide. Thus, ethidium bromide was acylated by Ph chloroformate in a mixture of 500 mM sodium phosphate buffer (pH 6.6) and acetone at room temperature for 10 min to give 3,8-bis(phenoxycarbonylamino)-6-phenyl-5-ethylphenanthridinium dihydrogenphosphate which was heated with NH3 in methanol in a pressure tube at 80° for 1 h to give 3,8-di(ureido)-6-phenyl-5-ethylphenanthridinium chloride (III). III in vitro showed the binding affinity to DNA with Kd of 106, μM, IC50 of >1/0 μM μg/mL against HIV-1 rev response element, IC50 of 15 μM against HIV-1, and exhibited no toxicity against HeLa cells at 10 μM.

IT 660836-33-9P, 3-[N,N'-Bis(tert-butoxycarbonyl)guanidino]-8-(benzyloxycarbonylamino)-6-phenyl-5-ethylphenanthridinium chloride
660836-37-3P, 8-[N,N'-Bis(tert-butoxycarbonyl)guanidino]-3-(benzyloxycarbonylamino)-6-phenyl-5-ethylphenanthridinium chloride
845858-38-0P, 3,8-Bis[N,N'-bis(tert-butoxycarbonyl)guanidino]-6-phenyl-5-ethylphenanthridinium chloride
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phenanthridine derivs. with selective viral nucleic acids-binding property as antiviral agents)

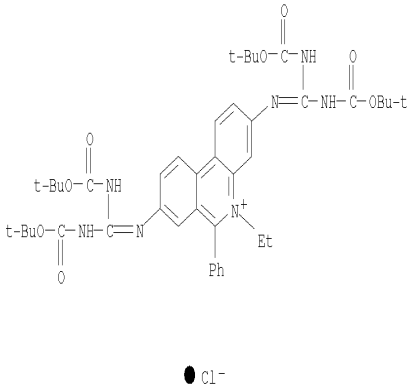
RN 660836-33-9 CAPLUS
CN Phenanthridinium, 3-[[bis[[(1,1-dimethylethoxy)carbonyl]amino]methylene]amino]-5-ethyl-6-phenyl-8-[[(phenylmethoxy)carbonyl]amino]-, chloride (9CI) (CA INDEX NAME)



RN 660836-37-3 CAPLUS
CN Phenanthridinium, 8-[[bis[[(1,1-dimethylethoxy)carbonyl]amino]methylene]amino]-5-ethyl-6-phenyl-3-[[(phenylmethoxy)carbonyl]amino]-, chloride (9CI) (CA INDEX NAME)



RN 845858-38-0 CAPLUS
CN Phenanthridinium, 3,8-bis[[bis[[(1,1-dimethylethoxy)carbonyl]amino]methylene]amino]-5-ethyl-6-phenyl-, chloride (9CI) (CA INDEX NAME)

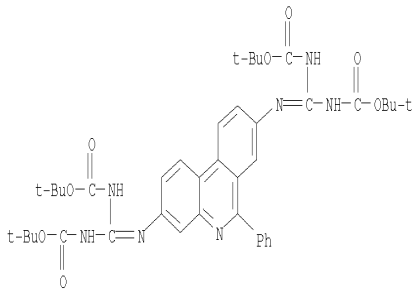


L4 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
2005:36679 Document No. 142:275617 Molecular Determinants for DNA Minor Groove Recognition: Design of a Bis-Guanidinium Derivative of Ethidium That Is Highly Selective for AT-Rich DNA Sequences. Bailly, Christian; Arafa, Reem K.; Tanious, Farial A.; Laine, William; Tardy, Christele; Lansiaux, Amelie; Colson, Pierre; Boykin, David W.; Wilson, W. David (INSERM U-524 et Laboratoire de Pharmacologie Antitumorale du Centre Oscar Lambret, IRCL, Lille, 59045, Fr.). Biochemistry, 44(6), 1941-1952 (English) 2005. CODEN: BICHAW. ISSN: 0006-2960. OTHER SOURCES: CASREACT 142:275617. Publisher: American Chemical Society.

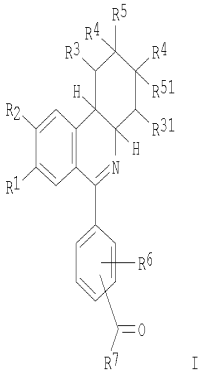
AB The phenanthridinium dye ethidium bromide is a prototypical DNA intercalating agent. For decades, this anti-trypanosomal agent has been known to intercalate into nucleic acids, with little preference for particular sequences. Only polydA-polydT tracts are relatively refractory to ethidium intercalation. In an effort to tune the sequence selectivity of known DNA binding agents, we report here the synthesis and detailed characterization of the mode of binding to DNA of a novel ethidium derivative possessing two guanidinium groups at positions 3 and 8. This compound, DB950, binds to DNA much more tightly than ethidium and exhibits distinct DNA-dependent absorption and fluorescence properties. The study of the mode of binding to DNA by means of circular and elec. linear dichroism revealed that, unlike ethidium, DB950 forms minor groove complexes with AT sequences. Accurate quantification of binding affinities by surface plasmon resonance using AnTn hairpin oligomer indicated that the interaction of DB950 is over 10-50 times stronger than that of ethidium and comparable to that of the known minor groove binder furamidine. DB950 interacts weakly with GC sites by intercalation. DNase I footprinting expts. performed with different DNA fragments established that DB950 presents a pronounced selectivity for AT-rich sites, identical with that of furamidine. The replacement of the amino groups of ethidium with guanidinium groups has resulted in a marked gain of both affinity and sequence selectivity. DB950 provides protection against DNase I cleavage at AT-containing sites which frequently correspond to regions of enhanced cleavage in the presence of ethidium. Although DB950 maintains a planar phenanthridinium chromophore, the compound no longer intercalates at AT sites. The guanidinium groups of DB950, just like the amidinium group of furamidine (DB75), are the critical determinants for recognition of AT binding sites in DNA. The chemical modulation of the ethidium exocyclic amines is a profitable option to tune the nucleic acid recognition properties of phenylphenanthridinium dyes.

IT 847361-44-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(bis-guanidinium derivative of ethidium is highly selective for AT-rich DNA sequences)

RN 847361-44-8 CAPLUS
CN Carbamic acid, [(6-phenyl-3,8-phenanthridinediyl)bis(nitrilomethanetetrayl)]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



L4 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
2004:182846 Document No. 140:235725 Preparation of 6-phenylphenanthridine derivatives as phosphodiesterase 4 (PDE4) inhibitors. Kley, Hans-Peter; Hatzelmann, Armin; Barsig, Johannes; Marx, Degenhard; Flockerzi, Dieter; Schmidt, Beate; Weinbrenner, Steffen (Altana Pharma A.-G., Germany). PCT Int. Appl. WO 2004018431 A2 20040304, 49 pp. DESIGNATED STATES: W: AE, AL, AU, BA, BR, CA, CN, CO, DZ, EC, EE, HR, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, SG, TN, UA, US, VN, YU, ZA, ZW; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-EP8967 20030813. PRIORITY: EP 2002-18530 20020817.
GI

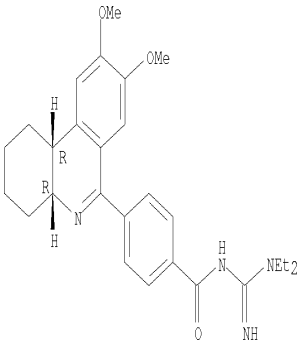


I

AB The title compds. [I; R1, R2 = HO, C1-4 alkoxy, C3-7 cycloalkoxy, C3-7 cycloalkylmethoxy or completely or predominantly fluorine-substituted C1-4 alkoxy; or R1 and R2 together are a C1-2 alkylenedioxy group; R3, R31 = H, C1-4 alkyl; or R3 and R31 together are a C1-4 alkylene group; R4 = H, C1-4 alkyl and R51 = H; or R5 and R51 together represent an addnl. bond; R6 = H, halogen, nitro, C1-4 alkyl, CF3, C1-4 alkoxy; R7 = (un)substituted guanidino, heterocyclylamino, 1-heterocyclyl-1-(imino)methyl, etc.] or salts thereof, as well as N-oxides, enantiomers, E/Z isomers, or tautomers thereof and their salts are prepared These compds. I are useful for producing pharmaceutical compns. for treating respiratory disorders and/or dermatoses. Also disclosed is a method for treating an illness treatable by administration of a PDE4 inhibitor in a patient comprising administering to said patient in need thereof a therapeutically effective amount of a compound of formula I, in particular airway disorders. N'-[1-[4-[(4aR,10bR)-8,9-Dimethoxy-1,2,3,4,4a,10b-hexahydrophenanthridin-6-yl]phenyl]methanoyl]-N,N-diethylguanidine. Thus, 4.9 g 1,1-diethylguanidinium sulfate was suspended in 120 mL MeCN, treated with 720 mg NaOH in 25 mL MeOH, and stirred at room temperature for 1 h. The solvent
was evaporated and the residue was suspended in 200 mL CH2Cl2, treated with 5.2 g Na2CO3 and then dropwise with a solution of 4.2 g 4-[(4aR,10bR)-8,9-

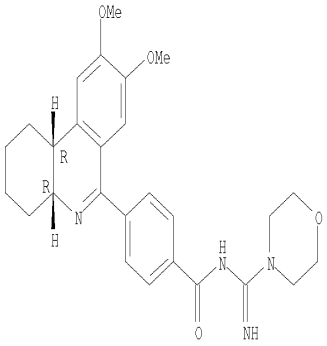
dimethoxy-1,2,3,4,4a,10b-hexahydrophenanthridin-6-yl]benzoyl chloride hydrochloride in 200 mL CH2Cl2 dropwise, and stirred at room temperature for 15 h to give, after workup and silica gel chromatog., N'-[1-[4-[(4aR,10bR)-8,9-Dimethoxy-1,2,3,4,4a,10b-hexahydrophenanthridin-6-yl]phenyl]methanoyl]-N,N-diethylguanidine (II). 12 Compds. I including II showed -logIC50 (mol/L) of >8 against phosphodiesterase 4.
IT 667422-55-1P 667422-57-3P 667422-58-4P
667422-59-5P 667422-61-9P 667422-62-0P
667422-63-1P 667422-64-2P 667422-65-3P
667422-66-4P 667422-67-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phenylphenanthridine derivs. as phosphodiesterase 4 (PDE4) inhibitors for treating respiratory disorders and/or dermatoses dermatosis)
RN 667422-55-1 CAPLUS
CN Benzamide, N-[(diethylamino)iminomethyl]-4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]- (CA INDEX NAME)

Absolute stereochemistry.



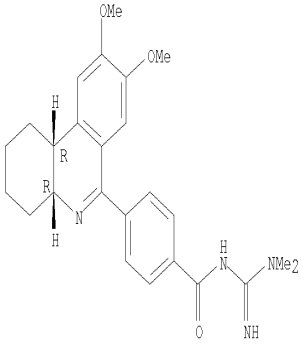
RN 667422-57-3 CAPLUS
CN Benzamide, 4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-(imino-4-morpholinylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.



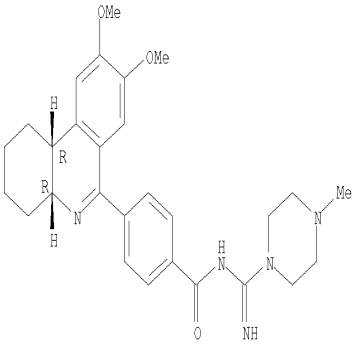
RN 667422-58-4 CAPLUS
CN Benzamide, N-[(dimethylamino)iminomethyl]-4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]- (CA INDEX NAME)

Absolute stereochemistry.



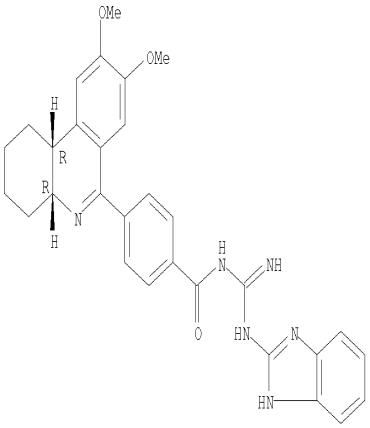
RN 667422-59-5 CAPLUS
CN Benzamide, 4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-[imino(4-methyl-1-piperazinyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



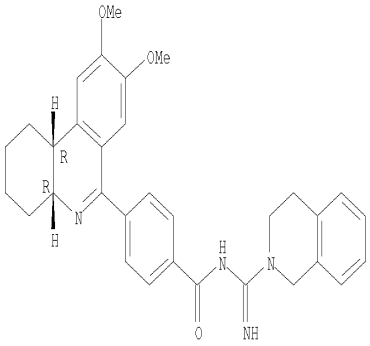
RN 667422-61-9 CAPLUS
CN Benzamide, N-[amino(1H-benzimidazol-2-ylamino)methylene]-4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



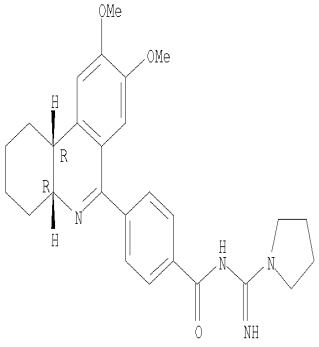
RN 667422-62-0 CAPLUS
CN Benzamide, N-[(3,4-dihydro-2(1H)-isoquinolinyl)iminomethyl]-4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]- (CA INDEX NAME)

Absolute stereochemistry.



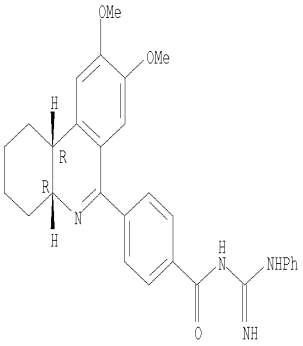
RN 667422-63-1 CAPLUS
CN Benzamide, 4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-(imino-1-pyrrolidinylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.



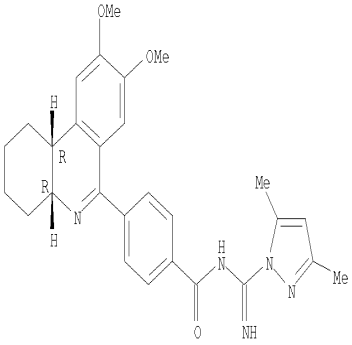
RN 667422-64-2 CAPLUS
CN Benzamide, 4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-[imino(phenylamino)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



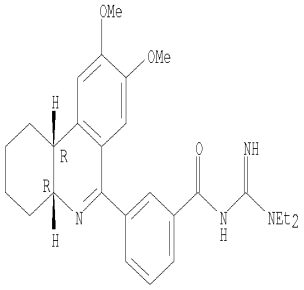
RN 667422-65-3 CAPLUS
CN Benzamide, N-[(3,5-dimethyl-1H-pyrazol-1-yl)iminomethyl]-4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]- (CA INDEX NAME)

Absolute stereochemistry.



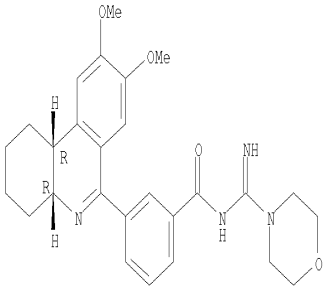
RN 667422-66-4 CAPLUS
CN Benzamide, N-[(diethylamino)iminomethyl]-3-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]- (CA INDEX NAME)

Absolute stereochemistry.



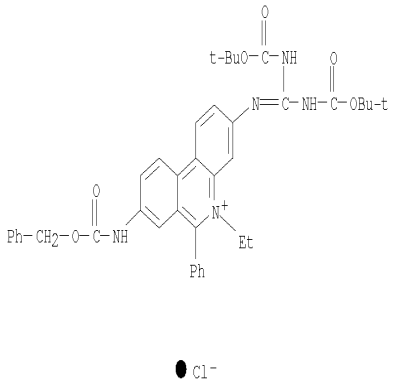
RN 667422-67-5 CAPLUS
CN Benzamide, 3-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-(imino-4-morpholinylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.

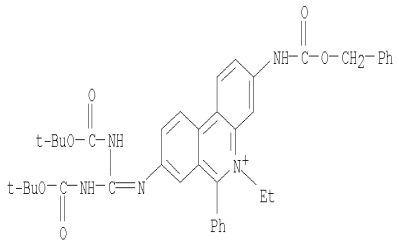


L4 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
2003:867286 Document No. 140:192208 Synthesis, photophysical properties, and nucleic acid binding of phenanthridinium derivatives based on ethidium. Luedtke, Nathan W.; Liu, Qi; Tor, Yitzhak (Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA, 92093-0358, USA). Bioorganic & Medicinal Chemistry, 11(23), 5235-5247 (English) 2003. CODEN: BMECEP. ISSN: 0968-0896. OTHER SOURCES: CASREACT 140:192208. Publisher: Elsevier Ltd..
AB In an attempt to decrease the DNA affinity (and hence the toxicity and mutagenicity) of ethidium bromide, a series of substituted phenanthridine derivs. has been synthesized by converting the amines at the 3- and 8-positions of ethidium bromide into guanidine, pyrrole, urea, and various substituted ureas. The resulting derivs. exhibit unique spectral properties that change upon binding nucleic acids. The compds. were analyzed for their ability to inhibit the HIV-1 Rev-Rev Response Element (RRE) interaction, as well as for their affinity to calf thymus DNA. One derivative (3,8-bis-urea-ethylenediamine-5-ethyl-6-phenylphenanthridinium

trifuroracetate) has an enhanced affinity and specificity for HIV-1 RRE as compared to ethidium bromide. These results indicate that the nucleic acid affinity and specificity of an intercalating agent can be tuned by synthetic modification of its exocyclic amines.
IT 660836-33-9P 660836-37-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis, photophys. properties, and nucleic acid binding of phenanthridinium derivs. based on ethidium)
RN 660836-33-9 CAPLUS
CN Phenanthridinium, 3-[[bis[[(1,1-dimethylethoxy)carbonyl]amino]methylene]amino]-5-ethyl-6-phenyl-8-[[(phenylmethoxy)carbonyl]amino]-, chloride (9CI) (CA INDEX NAME)



RN 660836-37-3 CAPLUS
CN Phenanthridinium, 8-[[bis[[(1,1-dimethylethoxy)carbonyl]amino]methylene]amino]-5-ethyl-6-phenyl-3-[[(phenylmethoxy)carbonyl]amino]-, chloride (9CI) (CA INDEX NAME)



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